

--12. (New) A method for designing a therapeutic useful for treating a genetic disease, said method comprising:

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- a) determining at least a portion of a nucleotide sequence of a mutant allele;
  - b) designing a suppression effector that binds to the portion of the nucleotide sequence, thereby to inhibit the expression of the mutant allele; and
  - c) designing a replacement nucleic acid which varies from the mutant allele by having one or more degenerate / wobble sites that are altered so that the replacement nucleic acid is not inhibited by the suppression effector,
- wherein the replacement nucleic acid encodes a wild-type or non-disease causing protein.

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13. (New) A method for designing a therapeutic useful for treating a genetic disease, the method comprising:

- a) determining at least a portion of a nucleotide sequence of a mutant allele;
- b) identifying the presence of a ribozyme cleavage site on the mutant allele;
- c) designing a ribozyme that cleaves an RNA encoded by the mutant allele; and
- d) designing a replacement nucleic acid which is not suppressed or is only partially suppressed,

wherein the replacement nucleic acid differs from the mutant allele in at least one degenerate / wobble position of at least one codon and wherein the replacement nucleic acid encodes a wild-type or non-disease causing protein.

14. (New) The method of claim 12, wherein the suppression effector is a nucleic acid or a peptide nucleic acid (PNA).

15. (New) The method of claim 12, wherein the suppression effector is a peptide or an antibody.

16. (New) The method of claim 12, wherein the suppression effector is a nucleic acid that forms a triple helix with the mutant allele.

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17. (New) The method of claim 12, wherein the suppression effector is an antisense nucleic acid.

18. (New) The method of claim 12, wherein the suppression effector is a single-stranded RNA.

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cont

19. (New) The method of claim 12 or 13, wherein the suppression effector is a ribozyme which cleaves an RNA encoded by the mutant allele.

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20. (New) The method of claim 19, wherein the ribozyme cleaves an RNA encoded by the mutant allele at an NUX ribozyme cleavage site.

21. (New) The method of claim 12 or 13, wherein the suppression effector is operatively linked to an expression vector.

22. (New) The method of claim 12 or 13, wherein the suppression effector binds to the mutant allele in one or more sites selected from the group consisting of a coding region, a 5' untranslated region, a 3' untranslated region and an intronic region.

23. (New) The method of claim 12 or 13, wherein the genetic disease is an autosomal dominant disease or a polygenic disease.

24. (New) The method of claim 12 or 13, wherein the genetic disease is osteogenesis imperfecta, retinitis pigmentosa, age-related macular degeneration, glaucoma, manic depression or cancer.

25. (New) The method of claim 12 or 13, wherein the replacement nucleic acid encodes a protein selected from the group consisting of mammalian rhodopsin, collagen 1A1, collagen 1A2 and peripherin.

26. (New) The method of claim 12 or 13, wherein the replacement nucleic acid is operatively linked to an expression vector.

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C2) 27. (New) The method of claim 26, wherein the expression vector is a viral expression vector.  
cont

28. (New) A therapeutic designed for treating a genetic disease linked to a mutation in a gene, comprising:

a suppression effector that suppresses the expression of a mutant allele; and

a replacement nucleic acid which differs from the mutant allele in at least one degenerate / wobble position of at least one codon and wherein the replacement nucleic acid encodes a wild-type or non-disease causing protein.

29. (New) A therapeutic designed for treating a genetic disease linked to a mutation in a gene, comprising:

a ribozyme that cleaves an RNA encoded by the mutant allele; and

a replacement nucleic acid which is not suppressed or is only partially suppressed, wherein the replacement nucleic acid differs from the mutant allele in at least one

degenerate / wobble position of at least one codon and wherein the replacement nucleic acid encodes a wild-type or non-disease causing protein.

30. (New) The therapeutic of claim 28, wherein the suppression effector is a nucleic acid or a peptide nucleic acid (PNA).

31. (New) The therapeutic of claim 28, wherein the suppression effector is a peptide or an antibody.

32. (New) The therapeutic of claim 28, wherein the suppression effector is a nucleic acid that forms a triple helix with the mutant allele.

33. (New) The therapeutic of claim 28, wherein the suppression effector is an antisense nucleic acid.

34. (New) The therapeutic of claim 28, wherein the suppression effector is a single-stranded RNA.

35. (New) The therapeutic of claim 28, wherein the suppression effector is a ribozyme which cleaves an RNA encoded by the mutant allele.

36. (New) The therapeutic of claim 35, wherein the ribozyme cleaves an RNA encoded by the mutant allele at an NUX ribozyme cleavage site.

37. (New) The therapeutic of claim 28 or 29, wherein the suppression effector is operatively linked to an expression vector.

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38. (New) The therapeutic of claim 28 or 29, wherein the suppression effector binds to the mutant allele in one or more sites selected from the group consisting of a coding region, a 5' untranslated region, a 3' untranslated region and an intronic region.

39. (New) The therapeutic of claim 28 or 29, wherein the genetic disease is an autosomal dominant disease or a polygenic disease.

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40. (New) The therapeutic of claim 28 or 29, wherein the genetic disease is osteogenesis imperfecta, retinitis pigmentosa, age-related macular degeneration, glaucoma, manic depression or cancer.

41. (New) The therapeutic of claim 28 or 29, wherein the replacement nucleic acid encodes a protein selected from the group consisting of mammalian rhodopsin, collagen 1A1, collagen 1A2 and peripherin.

42. (New) The therapeutic of claim 28 or 29, wherein the replacement nucleic acid is operatively linked to an expression vector.

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43. (New) The therapeutic of claim 42, wherein the expression vector is a viral expression vector.

44. (New) A kit comprising a therapeutic for the treatment of a genetic disease linked to a mutation in a gene, the kit comprising: